# Non-invasive Assessment of Cardiovascular Mechanics Using a New, User-Friendly Software Application

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## ABSTRACT

*Currently, in most non-invasive imaging laboratories, echocardiographic tracings are interpreted by "eyeballing" M-mode and 2-dimensional echocardiographic recordings. This subjective method of data analysis severely hampers the possibility of serial assessment of physiological interventions on cardiovascular disease states. Moreover, acquisition of important cardiovascular physiological data usually requires recordings of instantaneous aortic pressure and flow data that, until recently, could only be acquired invasively in the cardiac catheterization laboratory. Recently, our laboratory has developed and validated new "non-invasive" methods for the acquisition of aortic pressure and flow using calibrated subclavian pulse tracings and continuous wave aortic Doppler, respectively [1-3].*

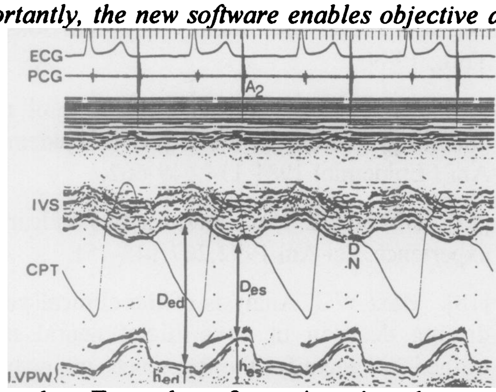
*With these limitations and new developments in mind, we developed new software that enables simultaneous non-invasive acquisition of left ventricular (LV) chamber geometry and aortic pressure and flow data. This new, user-friendly software in conjunction with other non-invasive tools allows non-invasive quantification of multiple cardiovascular physiological parameters. More importantly, the new software enables objective and serial assessment of multiple pharmacological interventions on various patients' disease states.*

## INTRODUCTION

The possession of a non-invasive tool that allows for objective serial quantification of overall LV cardiovascular function may be extremely useful for physicians. It would assist in managing patients with cardiovascular diseases. By assessing and understanding the underlying physiological principles governing the cardiovascular system, one might be better able to grasp the pathophysiology of a given disease state as well as the results of therapeutic interventions.

We have tried to create such a non-invasive tool by developing a computer program that acquires LV physiological data from a digitizing tablet. Simultaneously acquired 1) LV chamber dimensions and wall thicknesses obtained from cardiac ultrasound imaging (two-dimensional targeted M-mode echocardiographic tracings), 2) aortic flow from quantitative continuous wave aortic Doppler, and 3) aortic pressure obtained from externally recorded calibrated subclavian pulse tracings are sequentially digitized onto a commercially available data tablet. The tablet is connected to the serial port of a 486 personal computer.

(a)




(b)

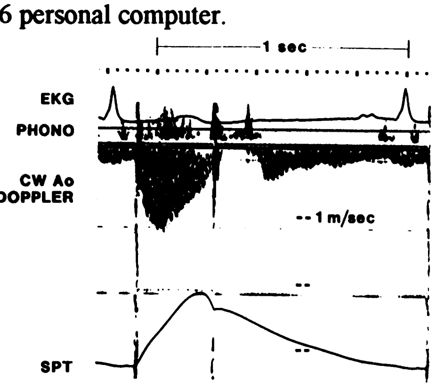



Figure 1. Examples of non-invasive data traced on a digitizing tablet. a) Simultaneous recordings of electrocardiogram (ECG), phonocardiogram (PCG), and 2D-targeted M-mode echocardiogram; IVS = interventricular septum, CPT = carotid pulse tracing, Ded = end-diastolic dimension, Des = end-systolic dimension, DN = dicrotic notch, LVPW = left ventricular posterior wall, hed = end-diastolic thickness, hes = end-systolic thickness. b) Simultaneous recordings of electrocardiogram (EKG), phonocardiogram (PHONO), continuous wave aortic Doppler (CW Ao DOPPLER), and subclavian pulse tracing (SPT).

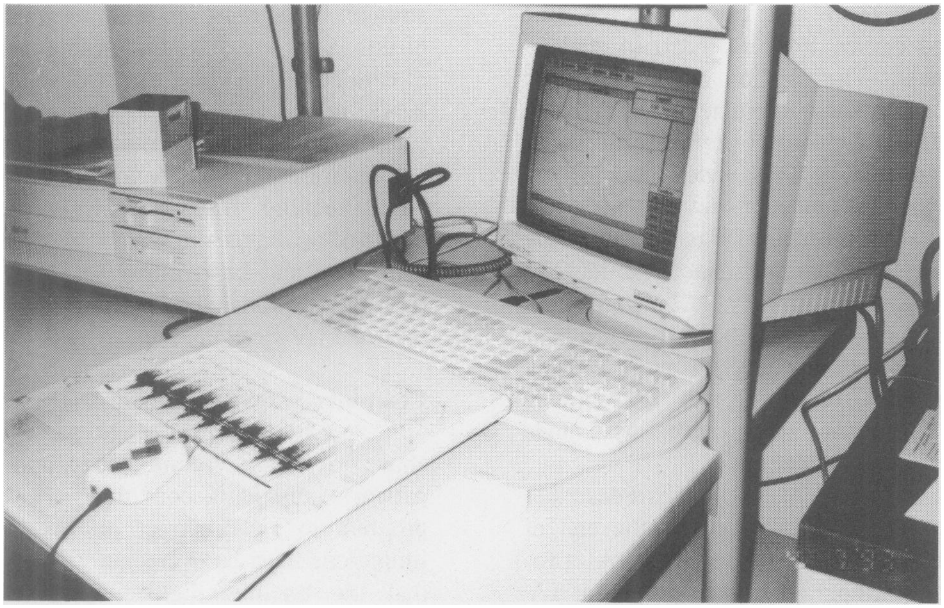


Figure 2. Example setup for using the Son of Digitizer in the echocardiology lab.

This newly developed software application enables the combination of cardiac ultrasound imaging, quantitative Doppler echocardiography, and calibrated external pulse tracings to provide a powerful set of tools for the analytic assessment of LV performance. This software application provides hemodynamically important data on myocardial mechanics, LV energetics, and cardiac systemic arterial coupling. The long-range clinical goal of this software application is to provide the researcher and clinician with new insights into the underlying pathophysiology of cardiovascular disease processes in order to facilitate management and replace empirical therapy with more rationally based therapy.

**Physiology and Imaging Background**

The cardiovascular system is an integrated functional unit having two major components (i.e., left ventricle and systemic circulation) that are interfaced by a complex series of biophysical feedback mechanisms. On the ventricular side, overall LV systolic performance (e.g., ejection fraction, stroke volume) reflects the net effect of the interplay between afterload, preload, heart rate, and LV contractility. Afterload and preload, the forces acting on the LV fibers at end-systole and end-diastole respectively, are best quantified using circumferential wall stress. During ventricular systole, the LV cavity and the systemic arterial circulation are in continuity. As seen in Figure 3, flow and pressure are the physiologic mediators that connect the heart and the systemic circulation. The load imposed on the ventricle is a function of both cardiac properties and vascular factors (i.e., systemic vascular resistance and arterial compliance) that impede the forward flow of blood [1, 4, 5].

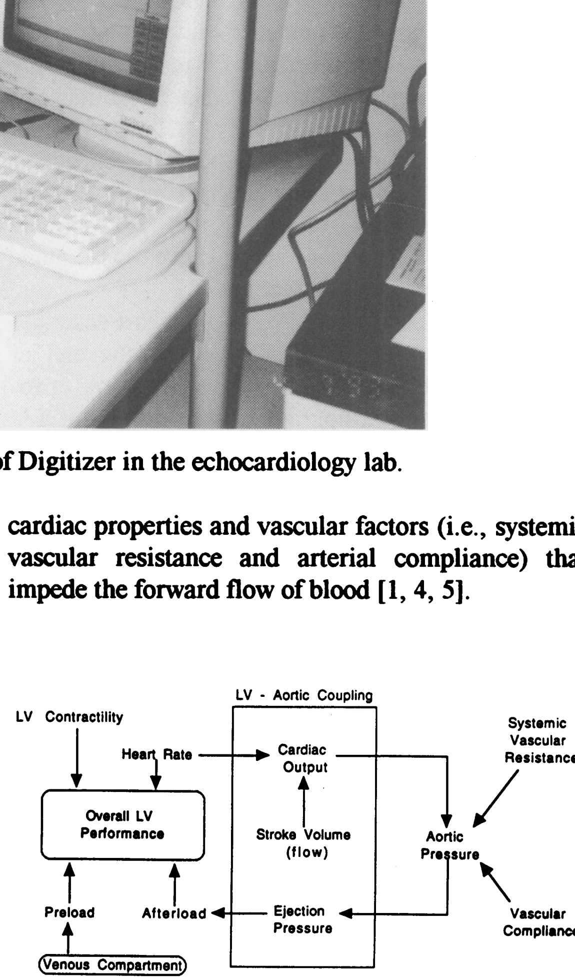



Figure 3. Physiological framework for the analysis of myocardial mechanics, left ventricular energetics, and cardiac-systemic arterial coupling.

**Cardiac Performance.** Cardiac performance reflects the net interaction of many physiologic parameters. When represented by output flow of the left ventricle (i.e., cardiac output), there are four major determinants: 1) heart rate, 2) preload, 3) afterload, and 4) LV myocardial contractility. All of these variables can be analyzed by using the previously described methods.

By combining echocardiography measurements of the aortic root cross sectional area with Doppler, it is possible to calculate the heart's stroke volume (the volume of blood ejected from the heart every heart beat) and cardiac output (the volume of blood ejected from the heart in a given amount of time). The ejection fraction (EF) is defined as the ratio of stroke volume to end-diastolic volume and reflects the overall performance of the cardiovascular system. This index is also an important prognostic indicator in patients with cardiac disease. However, since EF is not commonly measured with echocardiography (since end diastolic volume can only be roughly estimated), the fractional shortening (FS) of the left ventricular diameter can be substituted. FS is an index that correlates very well with EF and is routinely calculated in patients who have M mode echocardiography examination [6, 7].

**Preload.** The preload of the heart describes the forces acting on the LV fibers at the end of diastole. This is best appreciated by two-dimensional echocardiography visualization of LV size during end-diastole. The chamber size is much more reliable than chamber pressure for this determination.

**Afterload.** All factors that impede cardiac ejection in the arteries constitute afterload. The precise study of afterload requires sophisticated mathematical analysis of instantaneous pressure-flow relationships found in the aorta. The non-invasive acquisition of this information has proved to be a major improvement when approaching patients with cardiovascular disease (who were previously considered ineligible for cardiac catheterization).

**Left Ventricular Wall Stress.** LV wall stress is directly related to the afterload during ejection. By combining M mode echocardiography measurements of LV diameter and thickness together with aortic pressure data, one can calculate the LV wall stress over the cardiac cycle. Furthermore, since the integral of LV wall stress is a major determinant of myocardial oxygen consumption, indices like "ejection stress integral" and "stress time" may be computed when investigating the energy requirements of the heart [8].

**Cardiac mass.** Cardiac mass can be calculated from M mode echocardiography measurements of LV wall thickness. This parameter may be important when considering how the heart compensates for different afterload conditions. For example, a patient with hypertension will have a consistently high LV peak wall stress, and the thickness of the walls will increase to normalize this elevated value.

**Contractility.** Contractility is an intrinsic characteristic of heart muscle that represents the true strength of the muscle fibers. In vivo measurements of this factor are difficult due to other determinants of cardiac performance (i.e., loading conditions and heart rate). However, the use of M mode echocardiography has provided an adequate method of determining the "velocity of shortening of circumferential fibers" (VCF), which is highly sensitive to changes in contractility but independent of preload and heart rate. VCF can be calculated from the fractional shortening of the heart, the heart rate, and LV ejection time.

**Computer Software - Son of Digitizer**

All of the physiologic parameters discussed above may be useful in better understanding the patient's underlying condition. However, for this program to yield correct information, two major limitations must be overcome. First, it is necessary that the tracings digitized with the tablet are physiologically correct and technically acceptable. The Son of Digitizer was created to interface with multiple echocardiography laboratory non-invasive tools of interest (i.e., Doppler, electrocardiographic tracings, and phonocardiograms). The major functions of this software are 1) to act as a data acquisition device (with the addition of the digitizing tablet), 2) to perform all necessary calculations and create graphics for instantaneous results of studies, and 3) to reduce the inaccuracy of analysis by averaging multiple cardiac cycles.

## DATA ACQUISITION USING THE SON OF DIGITIZER

Initially, the user digitizes the important channel data of interest: the LV septal border, the endocardial and epicardial borders, EKG information, and the pressure pulse wave. A few heartbeats at a time can be traced on a single sheet that can be placed on the digitizing tablet for analysis.

The data tablet is connected via a serial port to a 486 based personal computer that is running The Son of Digitizer application (which was written in object oriented C++ for Windows). The software acquires data by the user tracing the stylus over each channel. Functions are built in to handle the incoming data to assure a good transformation of data from the tablet into the computer memory. This is accomplished by the computer forcing the user to trace in one direction, so that the corresponding channel data is a true function. In addition, raw data is run through a filter. This involves data points being interpolated so that elements of data fall into discrete time points independent of random speeds of human tracing.

The actual steps performed in collecting data are simple. Initially, calibrations are performed so the computer knows the orientation of the paper, the units of time on the vertical axis, and the units of the horizontal axes for the different channels. Then, each channel data can be traced. Each channel tracing is initiated by a button on the stylus. As the user traces each channel, a representation of the data is displayed on the screen for immediate feedback. After the channel has been traced, another button press will end the recording. Finally, several data points are selected that carry information which define the given heartbeat of interest (i.e., the dicrotic notch for when the aortic valve closes).

Since all of the data contained in the computer's memory is "virtual," it may be easily manipulated. For example, if pressure tracing data has been collected for 5 beats, an additional 'virtual channel' of data can be created to represent the average of these 5 channels of data. Another major advantage of the software is the capability of offsetting data along the time axis. This is important since there is a need to displace the pressure pulse tracing to accommodate the existing time delay between cardiac contraction and pulse transmission. In this case, data can be aligned by either of two methods. One option allows the user to drag the data so that a characteristic point in the curve (e.g., the dicrotic notch) lines up with other channel data. Alternatively, a time offset can be entered into the computer in milliseconds. Finally, data can be transplanted from one file to another by simple cutting and pasting in a similar way to other windows or Macintosh software.

Once the data has been successfully entered into the computer, multiple output features exist. A dialog box is displayed where the user can easily 'check off' any combination of items of interest on a list (a summary form and any of seven graphs). The summary form can be created that neatly lists the patient name, any comments, and all of the important variables of interest. In addition, graphs of certain variables (i.e., wall stress over time) can be automatically displayed or printed. Furthermore, if other graphs are of interest, there is a generic graphing option to graph any combination of channel data, including scatter plots. Lastly, any data collected can be stored to disk in two formats. One format allows for data to be read by the Son of the Digitizer or by Pegasus (software that can perform more extensive data analysis). The second format involves saving data as generic text, so that it may be imported into a spreadsheet.

Complements that have come from individuals familiar with the Son of Digitizer in the echocardiology lab include user friendliness and ease of use of the software. The program runs in Microsoft Windows version 3.1 and is entirely windows and popup-menus driven. A 'help bar' exists where instructions appear at the bottom of the application window for the user to follow. This includes directions on each step from the beginning calibrations until the end where data can be saved to disk. Another advantage of windows use is the Multiple Document Interface (MDI) capability. Multiple charts of data can be opened and manipulated at one time.

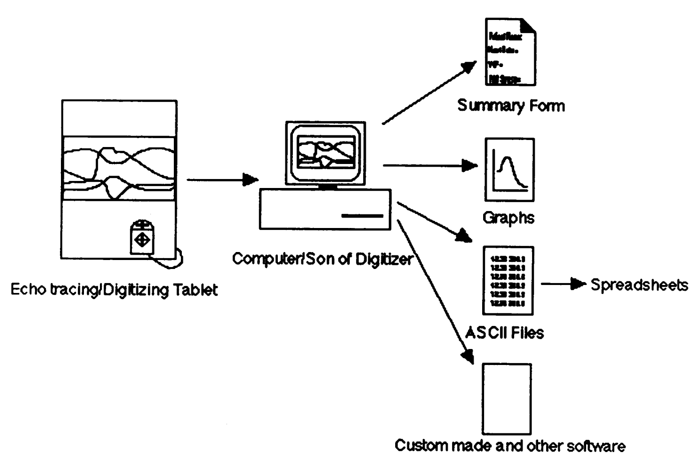
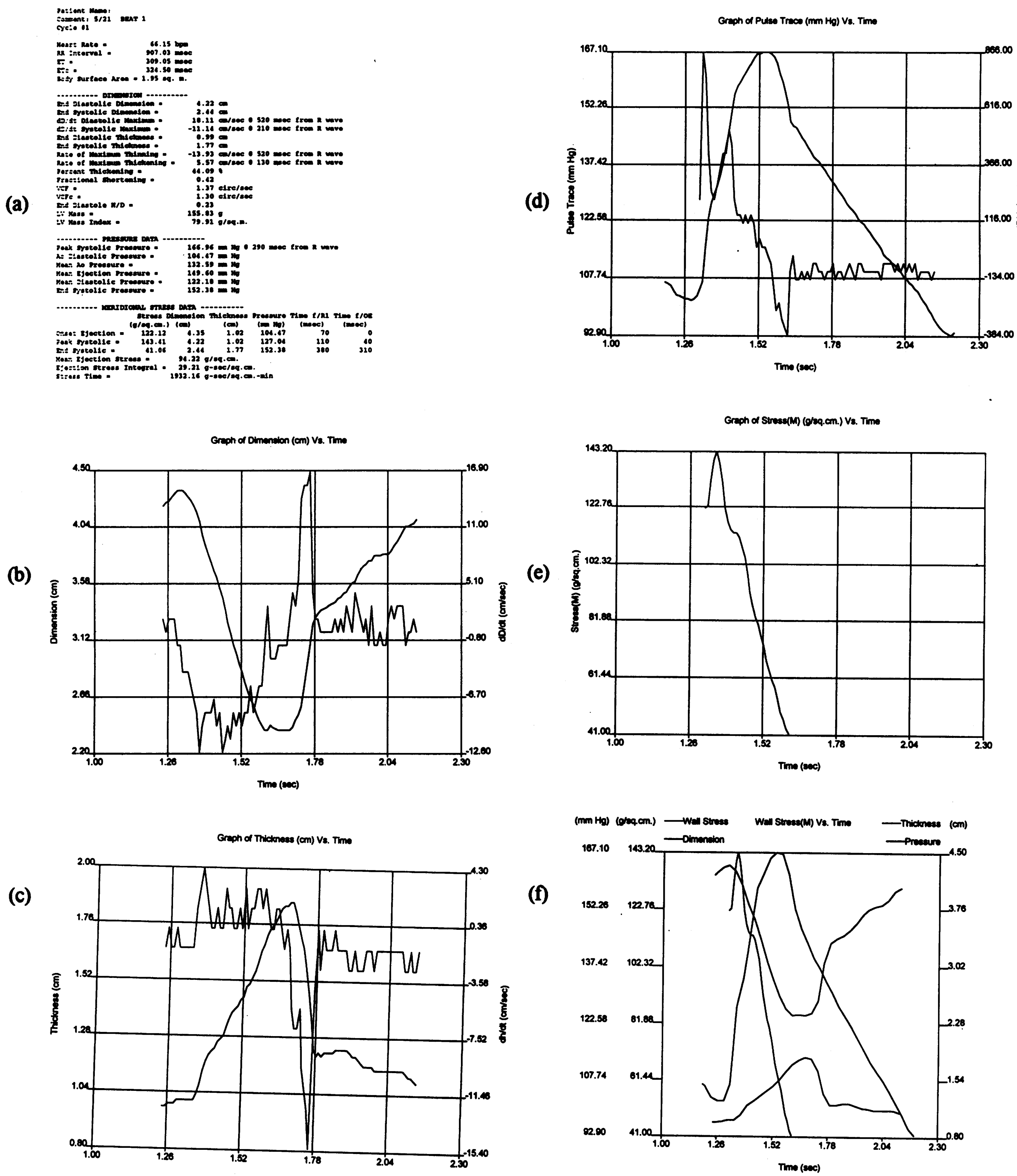



Figure 4. Schematic outlining the steps involved in data acquisition and analysis using the Son of Digitizer software application.



(a)

Patient Name:
Comment: 5/21 BEAT 1
Cycle #1

Heart Rate = 66.15 bpm
RR Interval = 907.03 msec
ET = 309.05 msec
ETc = 324.50 msec
Body Surface Area = 1.95 sq. m.

---------- DIMENSION ----------

| | | |
|---|---|---|
| End Diastolic Dimension = | 4.22 | cm |
| End Systolic Dimension = | 2.44 | cm |
| dD/dt Diastolic Maximum = | 18.11 | cm/sec @ 520 msec from R wave |
| dD/dt Systolic Maximum = | -11.14 | cm/sec @ 210 msec from R wave |
| End Diastolic Thickness = | 0.99 | cm |
| End Systolic Thickness = | 1.77 | cm |
| Rate of Maximum Thinning = | -13.93 | cm/sec @ 520 msec from R wave |
| Rate of Maximum Thickening = | 5.57 | cm/sec @ 130 msec from R wave |
| Percent Thickening = | 44.09 | % |
| Fractional Shortening = | 0.42 | |
| VCF = | 1.37 | circ/sec |
| VCFc = | 1.30 | circ/sec |
| End Diastole H/D = | 0.23 | |
| LV Mass = | 155.83 | g |
| LV Mass Index = | 79.91 | g/sq.m. |

---------- PRESSURE DATA ----------

| | | |
|---|---|---|
| Peak Systolic Pressure = | 166.96 | mm Hg @ 290 msec from R wave |
| Ao Diastolic Pressure = | 104.47 | mm Hg |
| Mean Ao Pressure = | 132.59 | mm Hg |
| Mean Ejection Pressure = | 149.60 | mm Hg |
| Mean Diastolic Pressure = | 122.18 | mm Hg |
| End Systolic Pressure = | 152.38 | mm Hg |

---------- MERIDIONAL STRESS DATA ----------

| | Stress (g/sq.cm.) | Dimension (cm) | Thickness (cm) | Pressure (mm Hg) | Time f/R1 (msec) | Time f/OE (msec) |
|---|---|---|---|---|---|---|
| Onset Ejection = | 122.12 | 4.35 | 1.02 | 104.47 | 70 | 0 |
| Peak Systolic = | 143.41 | 4.22 | 1.02 | 127.04 | 110 | 40 |
| End Systolic = | 41.06 | 2.44 | 1.77 | 152.38 | 380 | 310 |

Mean Ejection Stress = 94.22 g/sq.cm.
Ejection Stress Integral = 29.21 g-sec/sq.cm.
Stress Time = 1932.16 g-sec/sq.cm.-min



Figure 5. Sample output of the Son of Digitizer software application. a) Summary form with calculated parameters; b-e) Graphs of calculated variables versus time; f) Composite plot of stress and other variables versus time.

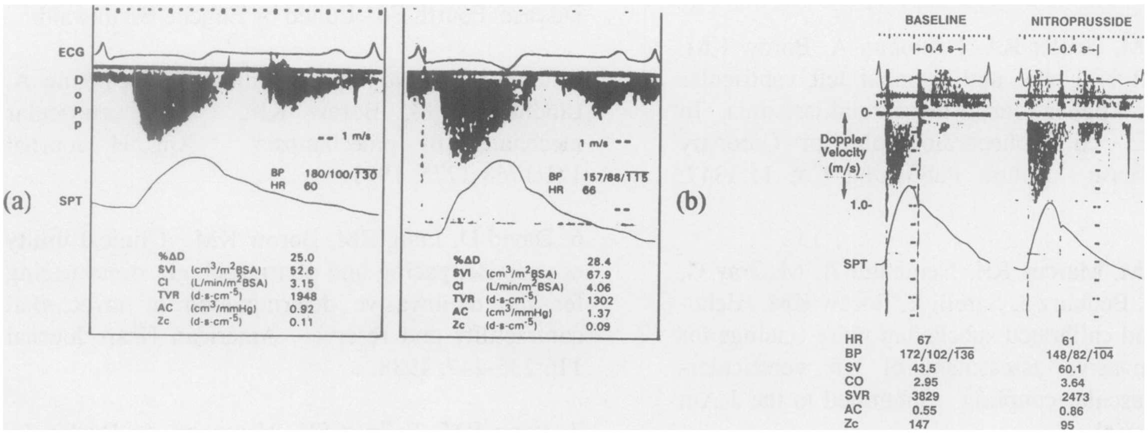



Figure 6. Non-invasively acquired pressure and flow measurements before and after treatment with a drug. a) Nicardipine in a patient with systemic hypertension. ECG = electrocardiogram; Dopp = continuous-wave Doppler; BP = blood pressure; HR = heart rate; % delta D = per cent fractional shortening; SVI = stroke volume index; CI = cardiac index; TVR = total vascular resistance; AC = arterial compliance; Zc = characteristic impedance. b) Nitroprusside in a patient with congestive heart failure. Dopp = continuous-wave Doppler; SPT = subclavian pulse tracing; HR = heart rate; BP = blood pressure; SV = stroke volume; CO = cardiac output; SVR = systemic vascular resistance; AC = arterial compliance; Zc = characteristic impedance [4].

## CLINICAL APPLICATIONS

With the aid of this new software application, the ventricular and vascular pathophysiological mechanisms in systemic hypertension and congestive heart failure can be identified. Figure (a) below shows the data recorded in a 46-year-old hypertensive woman at baseline and after 1 week of therapy of oral nicardipine. Under control conditions, total vascular resistance was elevated, LV percent fractional shortening was mildly depressed, and cardiac index was normal. After one week of antihypertensive therapy with nicardipine, it was observed that this therapy resulted in a decrease in external load resulting from beneficial alterations in total vascular resistance, arterial compliance, and characteristic impedance. Also, the integral of systolic wall stress decreased, suggesting a beneficial effect on myocardial energetics.

Figure (b) depicts the data acquired in a 69-year-old male with severe congestive heart failure. Using this application it was possible to obtain information on the cardiovascular effects of afterload reducing therapy. Nitroprusside resulted in beneficial hemodynamics as suggested by a decrease in heart rate, systemic vascular resistance, and characteristic impedance. In contrast, cardiac output and arterial compliance increased significantly.

## CONCLUSION

A new software package has been created that allows for simultaneous acquisition of various forms of non-invasive hemodynamic data. This application has proved to be a tool that is "user friendly" for both clinicians and researchers. The addition of this software package provides an excellent method for quantification of multiple cardiovascular physiological parameters.

As shown in this discussion, this application has already yielded clinically important information for patients regarding appropriate selection of therapy. The long range goal of this software program is to provide both the physician and cardiovascular researchers with new insights into the pathophysiology of cardiovascular disease.

## ACKNOWLEDGMENTS

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